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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/868,884	02/05/2002	Andrew Baxter	06275-233001	7953
7590	10/12/2005			
Janis K Fraser Fish & Richardson 225 Franklin Street Boston, MA 02110-2804			EXAMINER TRUONG, TAMTHOM NGO	
			ART UNIT	PAPER NUMBER
			1624	

DATE MAILED: 10/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/868,884

Applicant(s)

BAXTER ET AL.

Examiner

Tamthom N. Truong

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 13 July 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-3, 6-11 and 20-29 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1, 2, 6-11, 21-23 and 25-29 is/are allowed.
- 6) ☒ Claim(s) 20 and 24 is/are rejected.
- 7) ☒ Claim(s) 3 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_

### DETAILED ACTION

Applicant's amendment of 7-13-05 has been fully considered. The amended claim 9 has overcome the previous 112/2<sup>nd</sup> rejection, and thus, said rejection is withdrawn herein. The amended claims and argument have not overcome the previous rejections of 112/1<sup>st</sup> and 2<sup>nd</sup> paragraphs for claims 20 and 24. Therefore, said rejections are maintained.

Claims 4, 5 and 12-19 have been cancelled.

Claims 1-3, 6-11 and 20-29 are pending.

#### *Claim Rejections - 35 USC § 112, Second Paragraph*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 20 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a. Claim 20 remains rejected for an indefinite metes and bounds of a "*method of treating IKK2 mediated disease...*" because the specification does not provide a definite list of diseases mediated by IKK2. Applicant cited page 18, lines 10-18 for **examples** of IKK-2 mediated diseases. However, it is noted that many of the cited diseases do not manifest the same way, and affect several different organs. Furthermore, it is not clear if other diseases (not listed) are also intended.

b. Claim 24 remains rejected as being indefinite for reciting “multiple sclerosis” because claim 24 depends on claim 21 which recites “a method of treating an inflammatory disease, or a diseases with an inflammatory component”. However, the specification does not list “multiple sclerosis” as an inflammatory disease. The specification lists “multiple sclerosis” as one of many diseases “in which inhibition of IKK2 is beneficial”. In essence, claim 24 appears to lack antecedent basis.

***Claim Rejections - 35 USC § 112, First Paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. **Scope of Enablement:** Claims 20 and 24 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of an inflammatory disease, does not reasonably provide enablement for the treatment of other IKK-2 mediated disease or multiple sclerosis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The rejection is maintained for the reasons stated in the previous action and for the ones below:

a. Applicant asserted that: *“Since Applicants have described compounds that inhibit IKK2, it stands to reason that any IKK2-mediated disease may be amenable to treatment with the claimed compounds. The scope of claim 20 is perfectly aligned with what Applicants have enabled.”* However, the scope of claim 20 includes many diseases that affect several different organs such as: heart, lungs, immune system, AIDS, skin, bone, muscles, etc. All of the listed diseases do not share the same etiology, underlying factor, nor do they manifest the same way. In essence, claim 20 is a “reach through” claim.

b. Claim 24 is drawn to a method of treating multiple sclerosis (or MS). According to the Merck Manual, MS is a *“slowly progressive CNS disease characterized by disseminated patches of demyelination in the brain and spinal cord, resulting in multiple and varied neurologic symptoms and signs, usually with remissions and exacerbations.”* The Merck Manual further indicates that the *“cause is unknown but an immunologic abnormality is suspected, with few clues presently indicating a specific mechanism.”* Such a description clearly differentiates MS from the conventional “inflammatory diseases” which are known to be related to prostaglandins and leukotrienes. Therefore, the scope of claim 24 is not within the scope of claim 21, and is not enabled by the mere *in-vitro* data provided for the inhibition of IKK-2, which is the inhibitor of a serine threonine kinase.

c. Applicant further asserted that *“many if not all of the listed conditions have an inflammatory component that the Examiner apparently does not recognize: for example, multiple sclerosis, asthma, psoriasis, Grave’s disease, diabetes, and heart failure.”*

Asthma and psoriasis could be regarded as inflammatory diseases. However, as cited from the Merck Manual, MS is not an inflammatory disease. Likewise, diabetes is definitely **not** an inflammatory disease. Similarly, Graves's disease is a disease of hyperthyroidism, and **not** inflammation. Also, heart failure has never been linked to inflammation. Even if all those diseases are beneficial by the inhibition of IKK-2, there is no correlation between said inhibition with the lowering of blood sugar, blood pressure, or improving symptoms of MS, Graves's disease, etc. The mere fact that a compound can inhibit a kinase *in-vitro* does not sufficiently justify the treatment of a variety of diseases of no common etiology and manifestation tangentially related to IKK2 inhibition. The nexus between inhibition of IKK2 and disease treatment has not been sufficiently established.

d. A search in PubMed does not yield any reference teaching thiophene compounds as a class that can inhibit IKK2. A search in the US patent data base yields the reference of **Matsuo et.al.** (US 5,571,810) which teaches thiophene compounds as anti-inflammatory or analgesic agents. The anti-inflammatory effect shown in US'810 is that of arthritis. Thus, at most the state of the art only supports thiophene compounds in the treatment of an inflammatory disease like arthritis, and not even asthma, or psoriasis.

In short, with only *in-vitro* data provided in the specification and limited guidance from state of the art, the skilled clinician would have to carry out undue experimentation to use the claimed compounds in the treatment of various diseases as recited in claim 20, or in the treatment of MS as recited in claim 24.

***Claim Objections***

3. Claim 3 is objected to because of the following informalities: Claim 3 does not end with a period. Appropriate correction is required.

***Allowable Subject Matter***

4. Claims 1, 2, 6-11, 21-23, and 25-29 are allowed. The following is a statement of reasons for the indication of allowable subject matter:

Claims 1, 2, 6-11 are drawn to compounds of *(aminocarbonylamino)-thiophenecarboxamide* substituted with an optionally substituted phenyl group, and preparation thereof. Claims 21-23 and 25-29 are drawn to a method of treating an inflammatory disease, and pharmaceutical composition of the above compounds.

The prior arts of record fail to teach or fairly suggest a thiophene compound substituted with an unsubstituted carboxamide, an unsubstituted *(aminocarbonylamino)* (or urea), and a phenyl group.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



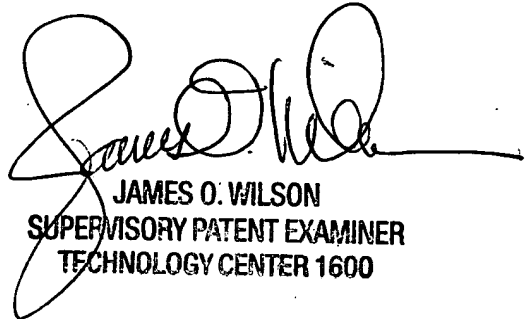
*Tamthom N. Truong*

*Examiner*

*Art Unit 1624*

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9-29-05



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